Letters to the editor

AN EIGHT-WEEK, OPEN-LABEL, PROSPECTIVE CASE SERIES OF ACAMPROSATE CALCIUM AS MONOTHERAPY FOR PATIENTS WITH COMORBID ANXIETY SYMPTOMS AND ALCOHOL MISUSE: AN EVALUATION FOR ALCOHOL SOBRIETY AND ANXIOLYSIS

DEAR EDITOR:

Anxious, alcohol-misusing patients are often treated with selective serotonin reuptake inhibitor (SSRI) medications, which elevate serotonin and thus alleviate anxiety. This often does not address continued alcohol use. Also, only about one third of anxious patients go into complete remission of their anxiety symptoms, and physicians often add benzodiazepine sedatives to completely treat patients to where they have no symptoms left.[1] Problematically, sedative-type drugs are associated with addiction and really cannot be used safely in the anxious, alcohol-misusing patient.

glutamate excess. This imbalance may instigate alcohol withdrawal and anxiety, both of which may cause a return to drinking to avoid withdrawal. Acamprosate is felt to restore the normal glutamate-GABA balance by dampening glutamate activity and helps patients lower their drinking and remain sober.

This GABA-glutamate balance is also felt to play a role in the development of anxiety. Low GABA and high glutamate levels (similar to the state of alcohol withdrawal) may be implicated. Often, GABA-promoting sedative drugs, are used to raise GABA activity to ward off anxiety symptoms. GABA sedatives are also used to treat alcohol withdrawal to restore balance over the short term. Given the similar glutamate-GABA imbalance in anxiety states and alcohol withdrawal states, acamprosate may be a likely candidate to treat the often comorbid conditions of alcohol misuse and anxiety.

This case series was designed to evaluate anxiety disorder (social anxiety, generalized anxiety, panic

> Our initial findings suggest that [acamprosate] may be reasonable for anxiety reduction and alcohol reduction in anxious, alcohol-misusing patients.

Acamprosate is a new US Food and Drug Administration (FDA) approved treatment that helps alcohol misusers abstain from drinking after becoming sober or detoxed.[2] It is felt that maintenance from alcohol consumption occurs when acamprosate is added to a patient's regimen. A difficult part of stopping alcohol consumption is the loss of GABA activity when alcohol intake stops in the face of remaining CNS

disorder) and alcohol-misusing (abuse or dependence) patients who had recently stopped drinking. Patients that were willing to cease drinking alcohol and be adequately detoxed (if warranted) were allowed into the study. No patient required benzodiazepine detoxification. All patients were able to cut alcohol use back gradually until they were five days sober and could enter the study. There was no evidence of withdrawal in any patient. Patients maintained all medically needed prescriptions during the study and no patient was taking any psychotropics at any time. This was a rater-blinded, patient open-label, prospective study, where all patients received acamprosate for eight weeks. This study was the first to date in a truly comorbid patient population, as the investigators utilized a comprehensive set of rating scales in order to best categorize patient responses in regards to anxiety, co-occurring depression, sleep disorders, alcohol use, and social functioning.

Following the baseline visit, patients began acamprosate treatment (two 333mg tablets, 3 times a day for the duration of the study). At the discretion of the investigaor, the dosage could be lowered for tolerability. Visits occurred at baseline and at the end of Weeks 1, 3, 5, and 8.

The total score from the Hamilton Rating Scale for Anxiety conducted at endpoint (Week 8 or early termination) was used to assess the overall efficacy of acamprosate for the treatment of anxiety. Secondary measures included: the Clinical Global Impression-Change (CGI), the proportion of patients in anxiety remission (defined as Hamilton-A total score ≤7), the change in the Sheehan Disability Scale (SDS), Pittsburgh Sleep Quality Index (PSQI), Hospital Anxiety and Depression Scale, the Alcohol Use Disorders Identification Test (AUDIT), and the Alcohol Timeline Followback (TLFB).

Five consecutive subjects enrolled and completed the study. In regards to our findings, the average age of the patients was 45 years and the average dose of acamprosate was 1,998mg/day (2 x 333mg tablets/3 times per day) during the eight-week study. Of the five patients who entered the study, four showed various levels of improvement in their anxiety levels as determined by the HAM-A and HADS

TABLE 1. Acamprosate results

		Median at		Distribution of Change (v5 minus v1)			
Variable	***N***	**V1**	**V5**	**25th**	**50th**	**75th**	***P*-value***
HAM-A	5	22	18	-2	-5	-17	0.0625
CGI-Severity	5	4	4	0	-1	-3	0.25
CGI-Global	5	N/A	3	4	3	1	0.0625
HADS							
Depression	5	12	10	0	-3	-9	0.25
Anxiety	5	12	10	0	-3	-9	0.25
AUDIT	5	24	20	-1	-1	-5	0.375
PSQI	5	14	8	-2	-5	-6	0.1875
TLFB	5	14	8	-2	-5	-6	0.1875

* The *P*-value was calculated from the Exact Wilcoxin Signed Rank test (2-sided).

scores. It was also found that four out of five patients had improved sleep and had somewhat reduced their consumption of alcohol based on the AUDIT scores.

This is the first known consecutive case series that initially attempts to evaluate the tolerability, feasibility, and potential effectiveness of the glutamate dampening agent, acamprosate, for treatment of anxiety and alcohol consumption issues simultaneously in truly comorbid patients. The drug was very well tolerated and all five subjects completed the study. Only one patient reported adverse effects (nausea and fatigue), which were mild and did not cause the patient to drop out. Given the small sample size and lack of control, this study is limited in its design. Our initial findings suggest that this product may be reasonable for anxiety reduction (Hamilton scores lowered an average of 18%, p=0.0625) and alcohol reduction (TLFB decreased 43%, p=0.1875). Future controlled studies may be warranted.

REFERENCES

1. Bellenger JC. Clinical guidelines for establishing remission in patients with depression and anxiety. *J Clin Psychiatry* 1999;60(Suppl 22):29–34.
2. Williams SH. Medications for treating alcohol dependence. *Am Fam Phys* 2005;72(9):1775–80.

With regards,
Thomas L. Schwartz, MD
Mark Chilton, MS
Alka Aneja, MD
All from Department of Psychiatry, SUNY Upstate Medical University, Syracuse, New York

Disclosure: After the completion of this study and acceptence for publication, Dr. Schwartz received a grant from Forest Laboratories to study acamprosate.

Address correspondence to:
Thomas Schwartz, MD, Associate Professor of Psychiatry, SUNY Upstate Medical University, Psychiatry Dept., 713 Harrison St., Syracuse, NY 13210; Phone: (315) 464-3166; Fax (315) 464-3163; E-mail: schwartzresearch1@yahoo.com